Environmental Endocrine Hypothesis and Public Policy

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In the summer of 1991 a group of scientists representing over a dozen disciplines met at the Wingspread Conference Center in Racine, Wisconsin, to share research findings pertaining to the effects of foreign chemicals on the reproduction and sexual development of humans and wildlife. A consensus statement reached by participants (referred to as the Wingspread Statement) asserted, in part, the following.[1]

> We are certain [that]:
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> A large number of man-made chemicals that have been released into the environment, as well as a few natural ones, have the potential to disrupt the endocrine system of animals including humans. Among these are the persistent, bioaccumulative, organohalogen compounds that include some pesticides (fungicides, herbicides, and insecticides) and industrial chemicals, other synthetic products, and some metals.
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> We estimate with confidence that:
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> Unless the environmental load of synthetic hormone disruptors is abated and controlled, large scale dysfunction at the population level is possible. The scope and potential hazard to wildlife and humans are great because of the probability of repeated and/or constant exposure to numerous synthetic chemicals that are known to be endocrine disruptors.

The Wingspread participants underscored the urgency of elevating the importance of reproductive effects in evaluating the health risks of industrial chemicals. Subsequent to the Wingspread Conference there have been sporadic accounts of the potential dangers of environmental hormone mimics and antagonists in the print and electronic media, two Congressional hearings on reproductive hazards and estrogenic pesticides,[1] and follow-up scientific meetings.[2,3] In essence, a public and environmental health advisory has been raised by a group of scientists who study different aspects of environmental endocrine disruptors and reproductive physiology in humans and animals. I shall refer to this advisory as the environmental endocrine hypothesis (EEH). For those interested in the relationship between science and policy, some of the salient issues are: How will the popular culture respond to these warnings? How will the legislative and regulatory sectors respond? What will the proponents of the Wingspread Statement have to do, scientifically or politically, to raise the

issues to a priority concern on the public agenda? There are some historical precedents and a body of social science research that may illuminate these questions.

This essay will address two aspects of the environmental endocrine hypothesis that bears on public policy. (1) What are the factors that determine whether a risk hypothesis gains a prominent place in the public agenda? (2) What are the current prospects within the regulatory sector for addressing the risks to the human endocrine system from a class of synthetic chemicals?

Hypothesis Formation and Public Policy

It is rare for scientists to organize themselves to advance a public health or environmental risk hypothesis. There are some notable exceptions. In 1975 biologists convened an international conference in California (the Asilomar Conference) to discuss potential hazards of recombinant DNA molecule research.[4] The meeting resulted in guidelines issued by the National Institutes of Health for genetic engineering research.

In another case, a group of atmospheric and environmental scientists, having first posited a relationship between chlorofluorocarbons (CFCs) and the depletion of atmospheric ozone, organized themselves as a force for changes in public policy.[5] One of the outcomes of this largely science-directed initiative was the signing of the Montreal Protocol in 1987, which included agreements on tighter quotas on the amount of CFCs the signatory nations are allowed to produce in any given year as well as heavy taxes on the continued use of the chemicals.[6] A third example of science-initiated risk hypotheses arose in the 1950s when physicists, biologists, and chemists (led by Linus Pauling) alerted the public that atmospheric testing of atomic weapons posed significant health risks to populations hundreds, even thousands, of miles from the test site.[7] Scientists went into the communities to alert citizens of the health risks of radioactive fallout products like carbon-14 and strontium-90, the latter of which was found in the milk of lactating mothers, as well as the bones and teeth of young children.[8]

In each of these cases, the scientific findings were only one of several factors that carried the hypothesis from scientific circles to the public policy arena, even while there was uncertainty over the risks, and in some cases no concrete evidence that there was a risk. The respective scientists who engaged in a public dialogue played multiple roles as generators, interpreters, and purveyors of knowledge and as advocates for policy change. There are many other instances where scientists at America's premier institutions trailed rather than led the advance of a risk hypothesis to a national policy forum. A recent example is found in the Alar episode. The chemical Alar (the trade name of daminozide) is a growth regulator used in preharvest fruits to establish uniformity in ripening and color. Alar was removed from use by farmers when the public stopped buying fruit treated with the chemical after a vigorous media exposé of the cancer-causing risks.[9] The issue was brought to the media and eventually to the public through the publication of a report assessing the cancer risks proposed by Alar to children. This report was prepared by the Natural Resources

Defense Council, a national public interest group that has fought for greater controls over the use of pesticides.[10] Typically, scientists continue the debate over the risks of a banned chemical years after regulatory action or a consumer boycott has occurred. This suggests that there are different action thresholds within science and public policy for reaching closure on risk hypotheses.

In the progress of scientific discovery it is usual for the validity of a hypothesis to remain in debate for many years before it is either rejected or incorporated into the canons of established knowledge. After 50 years of skepticism, scientists eventually adopted the hypothesis that plants can obtain nitrogen from the air.[11] A discussion of nitrogen fixation by bacteria that reside in the root nodules of plants appears routinely in basic biology texts ending years of skepticism that plants could only obtain nitrogen from soils.

It took the scientific community about 16 years before consensus was reached that CFCs were responsible for the breakdown of the protective ozone shield, with a detectable "hole" identified over Antarctica.[12] One can chart a gestation period for hypothesis formulation. In many cases, there is a preestablishment phase. A hypothesis may be advanced in the gray literature or in popular science publications but has not yet been published in mainstream journals. Once a hypothesis reaches the established science literature, a small group of adherents makes the case, advances the thesis in symposia, enters into debates in the journals, and seeks additional forms of evidentiary support. During this transitional period, the astute minds representing antagonists and protagonists create the tension and self-criticism that provide the quality control in science. The emergence of adversarial camps is central to ensuring that a hypothesis undergoes careful scrutiny before its final disposition. Criticism is indispensable to the growth and certification of knowledge.

The final phase in the life cycle of a hypothesis can take several forms. The status of the hypothesis may emerge clearly and definitively to the vast majority of the scientific community. Usually this occurs after new evidence appears in the form of a crucial experiment or critical discovery that plays a deciding role in the acceptance or rejection of the hypothesis. At other times, the fate of a hypothesis is determined slowly and incrementally. Proponents grow in numbers until a functional consensus emerges among leaders in the field. Like the Kuhnian paradigm shift, certain hypotheses finally are accepted into the canons of science when older skeptics retire or are outnumbered.

There is an important difference between the ozone hole and nitrogen fixation hypotheses. For most of its gestation period, the latter hypothesis was of interest to scientists exclusively. In contrast, from the outset, the ozone hole hypothesis had important public health and environmental policy implications. A reduction in atmospheric ozone could result in global radiation imbalances that might endanger the survival of species or at the very least cause increases in skin cancer. When a scientific hypothesis has important implications for public policy, the time needed to acquire definitive evidence of validity takes on a special significance. Ordinarily, science probes aggressively but waits patiently for nature to reveal her secrets. Partial evidence may be the stimulus for accelerated investigation. The literature is filled with causal

conjectures based on limited studies and inconclusive data. Some of these conjectures are eventually falsified, some remain dormant and fail to mobilize research interest from other investigators, and others serve as catalysts for focused research activity.

When a hypothesis describes a connection between a human activity and a public health effect of some consequence, it stands to reason it will draw concern from certain stakeholders and interest groups who seek a speedy resolution. Thus, a political context emerges that adds a trans-scientific value to the disposition of the hypothesis. Although nature is not apt to reveal her secrets on an earlier timetable because the knowledge obtained may reduce human suffering or protect the environment, public concerns may influence the social process of discovery. For example, additional resources may be allocated for accelerated data gathering. Certainly, the potential catastrophic consequences of ozone depletion brought widespread public pressure on resolving its conjectural status. Political pressure is inevitably reflected in the scientific community. Select constituencies begin to mobilize in support of mitigating action, even with limited evidence at hand. It may be rational to act "as if" the hypothesis were true even when the evidence is sparse. The assumption of taking action to diminish or eliminate a human activity that is weakly conjectured to have catastrophic effects is ostensibly an insurance policy.

However, from a public policy standpoint, it would be foolhardy to act on every hypothesis that describes an adverse outcome. First, the cost could be prohibitive. Some assurance is needed that there is a nontrivial probability of a significant effect. Second, competing hypotheses may confuse the plan of action and create social chaos. For example, there was the well-received hypothesis that chemical mutagens are likely human carcinogens. It has been reported in the scientific literature that ingredients in foods such as mustard, peanut butter, herb teas, and beer are mutagenic and therefore may be carcinogenic.[13] Policymakers acting on this hypothesis, who fail to consider alternative explanations, could bring about draconian regulations that erode confidence of the public in the integrity of science. Any scientific hypothesis is embedded in a wider system of beliefs. Similarly, an action principle in public policy must also consider multiple factors, such as the nature of the consequences if the hypothesis is true and no action is taken, the cost and effectiveness of strategies to mitigate the causal agent or agents, and the nature of the consequences if action is taken and the hypothesis is false.

The term "risk selection" refers to the social processes at work that elevate a risk hypothesis to the public agenda.[14] Rarely, if ever, is that accomplished exclusively by the aggregation of scientific knowledge. In 1948 dichlorodiphenyl trichloroethane (DDT) was cited in a widely publicized book as a potential hazard to the environment.[15] Fairfield Osborn was president of the New York Zoological Society, and the book had jacket reviews from Aldous Huxley, Robert Maynard Hutchins, and Eleanor Roosevelt. The author warned prophetically: "More recently a powerful chemical known as D.D.T. seems the cure all. Some of the initial experiments with this insect killer have been withering to bird life as a result of birds eating the insects that have been impregnated with the chemical. The careless use of D.D.T. can also result in destroying fish, frogs, and toads, all of which live on insects. This new chemical is deadly to many kinds of insects—no doubt of that. But what of the ultimate and net

result to the life scheme of the earth?" This was 14 years before Rachel Carson[16] completed *Silent Spring*. It took a talented science writer and the serialization of her book in the *New Yorker* to bring the issue of DDT into the light of public inquiry and another decade of debate before it was banned in the United States.

The concern over radioactive fallout from nuclear weapons testing brought little government action until strontium-90 was detected in humans. Dramatic discoveries of this type can provide the selective pressure that captures public imagination and transforms popular opinion into a powerful political force. These and other examples help us begin to understand the public response to a risk hypothesis. Sometimes it is a significant media event usually around human catastrophe (Bhopal, Love Canal, thalidomide) that sets Congress and the regulators in motion. In other cases such as ethylene dibromide (EDB), lead, dioxins, asbestos, no single event or discovery explains why federal actions are finally taken. It may be the sheer preponderance of evidence, litigation, media perseverance, and the dedicated work of a small group of unyielding advocates.

Current Regulatory Policy and Endocrine Disruptors

The general hypothesis I refer to as the environmental endocrine hypothesis posits a link between an operationally defined set of industrial and agricultural chemicals (such as xenobiotic estrogens) and endocrine-disrupting activity in vertebrates, including mammalian species. Conjectures about the relationship between synthetic chemicals and the endocrine system in fetal development were raised as early as 1979 according to Stone.[17] The environmental endocrine hypothesis in its broadest form serves a unifying role for a disparate class of reproductive and hormone-related pathologies in a variety of species. The messages communicated to the public in the environmental advocacy literature and the press are provocative and profoundly disturbing. They include: intersex features of male/female organs found in marine snails, fish, alligators, fish-eating birds, marine mammals, and bears; decline in sperm count by 50%; increased risk of breast cancer; small phalluses in Florida alligators resulting from pollution; penises found on female mammals; undeveloped testes in Florida panthers, masculinized female wildlife attempt to mate with normal females.[18]

The public policy ramifications of even a small subset of these outcomes is quite significant. Each of the subhypotheses is associated with an evolving body of evidentiary support. Thus, the general hypothesis is supported by a lattice of interconnecting but independent hypotheses of association. To date, despite the growing evidence, the environmental endocrine hypothesis cannot claim a single dramatic episode or discovery capable of turning public opinion into a sudden force for political change.

Nevertheless, there are effects cited by scientists that, in their view, represent a clear and present environmental danger. Among the most well-documented effects of endocrine disruptors is the dramatic reduction in the alligator population of Lake Apopka, Florida, the state's fourth largest body of fresh water. The lake was contam-

inated from years of pesticide runoff, effluent from a sewage treatment plant, and a pesticide spill. Alligator eggs collected from the lake were found to have concentrations of endocrine-disrupting chemicals, such as DDE, 10,000 times greater than what is normally found in the blood of newborn alligators.[19]

Another documented effect of endocrine antagonists is the disappearance of trout in the Great Lakes. The source of the problem has been traced to dioxin-like pollutants from industrial effluent.[18] Both examples point to inadequacies in the system of environmental regulation. For some endocrine disrupters like DDT and polychlorinated biphenyls (PCBs) that were implicated in these cases, regulatory actions have been taken. However, many other chemicals with endocrine-disrupting effects remain widely in use and merit immediate attention.

United States regulatory agencies have begun to take notice of the environmental endocrine hypothesis. The Environmental Protection Agency (EPA) and the Fish and Wildlife Service have called on the National Academy of Sciences to undertake a study of endocrine-disrupting chemicals.[20] The agency is supporting some research that seeks to understand the linkages between ecological impacts and human health impacts of xenobiotic chemicals. It is also collaborating with other agencies like the National Institutes of Health in an effort to understand the causal effects of estrogen-mimicking chemicals. However, before any regulatory initiative begins, if that should happen, it might be useful to consider the statutory authority of the relevant agencies to regulate environmental hormone modulators and the structural limitations of the existing regulatory framework.

I have already discussed the problems associated with elevating a risk hypothesis into the policy arena. Let us assume that in the not-so-distant future the conditions are such that, despite the antiregulatory mood in our country, a decision is made to regulate endocrine disruptors. To what extent are we prepared? Are the existing laws sufficient to address the issues? Will we be able to add this responsibility to the already heavily burdened regulatory system?

Several things can be said at the outset about regulatory policy toward hazardous substances. It has, for the most part, approached the management of hazardous substances chemical by chemical. Of the tens of thousands that have been introduced into agriculture and industrial production, very few chemicals have been explicitly banned from use and it may have taken decades to remove them. A few groups of chemicals are banned or their use is severely restricted. For example, PCBs are a class of chemicals that were banned for all manufacturing processes in 1979 whereas CFCs are being phased out of many products. These are the exceptions, however. Most regulated chemicals may be used within permissible limits.

Chemicals are regulated differently according to when they were introduced into commerce (some have been grandfathered in), by the type of use (food additives versus insecticides), by their putative effects (cancer-causing versus neurotoxic effects), by who is exposed (children versus workers).

There are six general ways that governments respond to the control of hazardous or potentially hazardous materials: conduct research; establish economic incentives for substitution or reduced use; enact legislation; issue regulations; undertake public education; or use moral persuasion (voluntary guidelines) to change consumption

or production patterns. The most publicized federal action on an estrogenic chemical occurred when the United States EPA banned the use of DDT in 1972 primarily because of its impact on the reproduction of birds. There was only conjectured evidence about the adverse effect of DDT on humans. The prohibition of DDT was rather unusual. Most pesticides that have been banned or severely restricted like chlordane or aldrin/dieldrin exhibited carcinogenic effects on mammals. Cancer and acute toxicity have been the dominant endpoints guiding the regulation of pesticides. In 1990, a report by the General Accounting Office (GAO) cited the insufficient attention given to reproductive toxicity by federal agencies. According to the GAO, at most 7% of the synthetic chemicals in use were tested to determine whether they harm the reproduction and development of animals.[21,22]

The EPA has two primary statutes that structure its regulatory course of action for chemical substances: they are the Federal Insecticide, Fungicide and Rodenticide Act (FIFRA) first passed in 1947 and amended in 1972 and the Toxic Substances Control Act (TSCA) enacted in 1976. The older and stronger of the two acts, FIFRA, is designed to regulate the use of pesticides. The 1972 amendments to FIFRA provided for premarket screening of pesticides. Manufacturers must demonstrate that a pesticide is not harmful to human health or to the environment prior to receiving a registration. However, there are several thousand formulations of pesticides already in use that have not been tested under the criteria established for new pesticides. Under a Congressional mandate, the EPA has been asked to reexamine the pesticides currently in use for their health and environmental impacts. Assessing chemicals for their effects on the endocrine system has not been an important part of the testing protocols for pesticides. However, it is within the authority of EPA under FIFRA to broaden the safety criteria according to which pesticides are evaluated. Prior to adding new criteria to its pesticide data requirements, the EPA would ordinarily prepare a scientific background paper justifying the action, convene a scientific advisory panel, and call for public comment to draft guidelines.

When TSCA was passed, there were about 30,000 chemicals in commerce. The EPA was given the authority to ban or restrict the manufacture, processing, distribution, commercial use, or disposal of any chemical substance or mixture that presents an unreasonable risk to human health or the environment. There are three main provisions of the act. The EPA may require testing of any chemical substance or mixture if it has reason to believe the chemical may present unreasonable risk. Prior notification is required for the manufacture of any new chemical substance (premanufacturing notice [PMN]) and for any manufacture or processing of an existing chemical substance for a significant new use. Finally, EPA may require record keeping and reports on chemical use and manufacture. The TSCA requirements are different for new and existing chemicals. Companies are required to issue a PMN before they can introduce a new chemical into production. The law gives the agency 90 days to review any new chemical that is being considered for industrial use. The agency uses limited criteria for the assessment of the chemical (for example, it frequently applies structure-activity analysis, which assumes chemicals with similar structures exhibit similar properties). The agency also maintains an inventory of about 70,000 chemicals currently in use. Many of these chemicals were grandfathered into use and were

not subject to rigorous assessments. In the first half decade TSCA was in effect, less than 10% of the new chemicals were subject to rigorous review.[23] The EPA receives about 1500 PMNs of new chemicals being produced each year and requires some form of testing in 10% of the cases.[24] A GAO study of TSCA reported that an EPA committee recommended a total of 386 substances for testing over a 14-year period and that the agency had complete test data for only six chemicals.[25]

Although EPA has statutory powers under TSCA to remove or limit a chemical from use, it must meet a significant burden to exercise its authority. The agency does not currently require endocrine disruption data in its review of TSCA inventory chemicals. Given the limited powers of TSCA, it will be difficult without some amendments to the law to add effective endocrine function assessment criteria to the current screening protocols. Moreover, TSCA is probably more responsive to cost-benefit considerations and proprietary constraints than either FIFRA or the food additive laws. Portney[26] notes: "The legislation [TSCA] has not been very effective, largely because there are no clear cut testing procedures or standards to determine whether a chemical does indeed present an imminent hazard, and because many companies have claimed that their products are proprietary—that they and only they have a right to know what the chemicals are."

With the prospect that an undetermined percentage of tens of thousands of chemicals in current use might be endocrine disruptors, the government is faced with a serious policy challenge. Some prioritization must be developed for screening chemicals currently in use. Under current case-by-case approaches in much of chemical regulation, it would take decades and substantial sums of money to meet a new set of regulatory goals based on the hazards of endocrine disruptors. According to Hynes,[27] "On paper both laws [TSCA and FIFRA] purport to solve the problems of preventing dangerous chemicals from being used commercially. At best, they keep only the worst new chemicals off the market." If the testing of carcinogens is any example, the definitive studies are costly and time-consuming. The preferred mammalian studies may take from 3 to 5 years to complete and cost upwards of $1 million per chemical.[23]

In a few notable cases regulatory agencies have attempted to group chemicals for more efficient regulation, departing from the substance-by-substance approach for setting health standards. PCBs, which were regulated by Congress and banned in 1976 after 46 years in production, are defined by a class of chlorinated synthetic organic compounds, namely, biphenyls (Ashford N: Personal communication, 1995). In 1973, the Occupational Safety and Health Administration (OSHA) issued emergency temporary standards and ultimately permanent standards regulating occupational exposures to a group of 14 carcinogens, representing chemicals used in the photographic and dye industry. The rulemaking and litigation associated with the rulemaking took 40 months. Subsequently, OSHA proposed a set of regulatory actions on carcinogenicity based on four generic categories. For example, proven carcinogens were to be based on two positive animal tests or one positive animal test and positive evidence from short-term assays. OSHA eventually issued an emergency temporary standard for such chemicals that met the carcinogen test. The generic approaches to regulating

chemicals spurred intense industry reaction and costly litigation. Eventually, the agency's approach to regulate groups of chemicals was brought into check by a new deregulatory mood.

More recently, bills have been introduced supported by environmental groups to phase out a large class of chlorinated organic compounds. Thus, the prospect of introducing a policy on regulating endocrine-disrupting compounds as a class is not unprecedented, but will be fought vigorously by manufacturers who would prefer substance-by-substance rulemaking. One early study noted that chemical regulation moves at a snail's pace "because the cumbersome statutory procedures provides a chemical with a full panoply of due process rights accorded to any individual in our constitutional system."[28] Our system of jurisprudence, which is grounded on individual rights, has found legitimacy for class action suits. Chemicals, as classes, may too gain status in regulatory decisions, but that has been the exception rather than the rule.

Even with a dependable, inexpensive, and short-term assay to identify xenobiotic hormone mimics or antagonists, along with evidence of causality, the decision on how they should be regulated could easily be mired in legal process. It is not sufficient to show that these chemicals can disrupt reproduction; it must be demonstrated that current exposures and doses pose an unreasonable risk to humans or wildlife. This may be accomplished either by demonstrating that this class of chemicals is the cause of past reproductive anomalies based on epidemiological data or through controlled laboratory experiments on human cells or animals. However, for most of the chemicals currently in commercial use the burden is on those who wish to restrict usage to demonstrate a causal effect.

Another problem facing regulators is how to address the by-products of chemicals that test negatively for endocrine-disrupting properties. Once emitted into the environment, these chemicals may recombine, in some instances producing metabolites that are hormone mimics or antagonists. The government's burden for regulating the commercial or industrial chemical sources of dangerous metabolites has always been high. For example, nitrosamine, a potent class of carcinogens, are a by-product of nitrites and nitrates which are used in processed meats. Sodium nitrate used as a preservative can react with amines in the stomach to produce nitrosamine. Regulators have argued that the benefits of the food additive in preventing botulism outweigh the risks of cancer. It is reasonable to assume that similar cost-benefit approaches will be applied to endocrine-disrupting chemicals. Unless regulators have a means to assess the potency of these chemicals on biological systems and their cumulative and combinatorial effects, the use of current laws may face insuperable obstacles.

Regulators will also be faced with the substitution dilemmas as they have had to address each time a product is banned or restricted. DDT and other pesticides developed in the 1940s and 1950s were replaced by chemicals that were less persistent in the environment but, in some cases, more toxic. Barring the elimination or phaseout of pesticides, regulators may see their role as being forced to choose between the lesser of two evils, a suspected carcinogen or an endocrine disruptor, a devil's gamble.

Restructuring the System of Chemical Regulation

The environmental endocrine hypothesis potentially covers a broad range and significant production quantities of structurally diverse chemicals. In some respects, the regulatory challenges for xenobiotics are like those for carcinogens, which also display wide variations in chemical structure. In contrast to carcinogens, for which there has been considerable attention within regulatory policy, far less attention has been given to managing endocrine disruptors. Although the knowledge of the causal mechanisms of disease would aid regulators, in the past chemicals have been restricted or banned when there was uncertainty about how a disease was caused. A case in point is asbestos regulation. Thus, for policymakers, the causal mechanism is less significant than some demonstration of causal pathology. Once there is consensus over cause and effect, policymakers must then assess the scope of the problem.

The process of chemical risk assessment has been slow and ponderous. It is estimated that toxicity information is unavailable for about 80% of the commercial chemicals.[23] The regulatory burden would be eased if the class of xenobiotics endocrine disruptors were small or if there were ample substitutes for the serious offenders. Currently, that class numbers about 45 synthetic chemicals, mostly pesticides. According to Wiles,[29] more than 220 million pounds of endocrine disruptors are applied to 68 different crops each year with atrazine (classified as a possible or probable human carcinogen by EPA) making up 29% of the total weight and 22% of the total acreage treated. Even without adding new demands on pesticide regulation, it is widely understood that the current system is inadequate to the task. Farmers, for example, are generally accorded a right to use an effective pesticide. Dorfman[30] notes: "the restrictions that are appropriate for any pesticide depend on the availability and effectiveness of substitutes."

It has become fashionable today to write about restructuring environmental regulation. Much of this trend is based on one or more of the conclusions that regulations are inefficient, irrational or illogical, unscientific, burdensome to industry, ineffective for protecting the public, and unresponsive to cost-benefit analysis. Many of the new critics support the conservative agenda that calls for downsizing federal regulations.

The emerging scientific evidence of endocrine-disrupting chemicals poses a challenge to the current regulatory system's capacity to manage a large-scale assessment of chemicals currently in commercial use that, ostensibly, have been grandfathered with regard to reproductive effects. It is also a challenge to an already overburdened system for testing and screening new compounds, and finally to international laws and treaties on transboundary disputes.

If we choose not to become mired in the slow pace of progress in the regulation of hazardous chemicals, some changes will have to be made in the fundamental way that our society evaluates new and existing synthetic compounds.

First, we will need to reach a consensus on effective and inexpensive assays for identifying endocrine disruptors and methods for assessing the human health risk of cumulative doses. In the past, agencies used different action criteria for deciding to

regulate or ban a chemical. Once assays are developed and validated, they should be applied uniformly to the 70,000 plus chemicals used in industrial production and the 600 plus active ingredients in pesticides.

Second, the standards of regulation should not depend on the route of exposure but rather on the amount of exposure. Endocrine disruptors that enter the food chain as pesticides should be regulated like food additives if their effects, such as reproductive toxicity, are comparable. Currently, there are two sets of de facto regulations, one applied to food additives and another to pesticide residues that place less controls on the latter. The Natural Resources Defense Council joined the State of California in filing suit against the EPA that argues the agency has failed to apply the 1958 Delaney amendment to dozens of pesticides that are known to cause cancer in animal studies. A recent settlement to the suit may remove 36 pesticides, but leaves open both the future of the Delaney amendment and its general application to pesticide residues.[31]

Third, we need an effective way to deal with endocrine disruptors that have become part of the waste stream through industrial effluent or pesticide runoff and that enter the food chain by absorption and concentration in marine organisms. This will require a reexamination of criteria pollutants under the Clean Water Acts where much of the emphasis has been on heavy metals, carcinogens, nitrates, and phosphates, and more recently PCBs and dioxins. Efforts to reduce the total environmental load of endocrine disruptors will also require amendments to FIFRA if it is shown that pesticides are a significant source of human exposure. Current information reveals a regulatory problem of significant scale, since it is estimated that more than 220 million pounds of pesticides known to be endocrine disruptors are applied to 68 different crops each year covering 225 million acres.[29]

Fourth, we must begin to address the problem of transnational food shipments where endocrine-disrupting chemicals may be introduced into United States markets at levels above those permitted in this country. Just a few years ago, an EPA administrator acknowledged that a minuscule number of imported bananas treated with benomyl (classified as an endocrine disruptor and a possible carcinogen) was inspected at the Mexican border. It is widely recognized that border inspectors, who are supposed to monitor pesticide residues on foreign produce, cannot meet the growing demand of imports as funds for inspectional services decline.

Fifth, TSCA must be strengthened if PMN requirements are to include mandatory screening for endocrine disruptors. The reporting and inventory requirements under TSCA could be amended to provide information on whether the chemicals currently in use are potentially endocrine disruptors in vertebrates.

Sixth, environmental regulations must address the issue of cumulative xenobiotic hormones from multiple chemical sources. The accumulated or lifetime exposures of individuals to particular chemicals have been factored into risk assessment models.[32] However, a system of regulation and risk assessment may have to take account of total xenobiotic chemical load originating from *different* agents if the additivity effect is confirmed in scientific experiments. This is a new challenge for regulators and will require an integrated look at chemicals. The closest analogy we have is with radiation standards. Annual and lifetime exposure limits have been established for workers in

the nuclear industry. A common metric for all sources of ionizing radiation along with the assumption that radiation risk is cumulative makes this regulation possible.

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QUESTIONS

1. What is the environmental endocrine hypothesis (EEH)?
2. Describe the system currently used in the United States to regulate chemicals, paying particular attention to the ways in which the system regulates, or fails to regulate, endocrine disruptors.